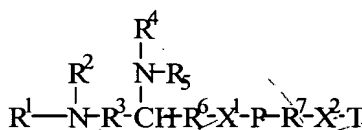


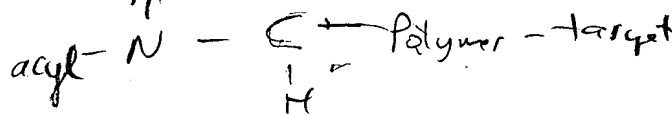
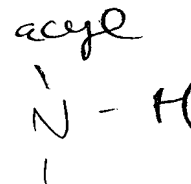
CLAIMS

What is claimed is:

1. A compound having the formula



(IV)



wherein:

X¹ and X² are independently a direct bond or a linking atom or group selected from the group consisting of -O-, -S-, -N(R⁸)-, -C(=X³)-, -C(=X³)-N(R⁸)-, -N(R⁸)-C(=X³)- and -C(=X³)-N(R⁸)-C(=X³)-;

X³ is -O- or -S-;

R¹ is acyl of from about 7 to about 23 carbons;

R² is hydrogen or lower alkyl;

R³ is a direct bond or alkylene of from 1 to about 10 carbons;

R⁴ is acyl of from about 7 to about 23 carbons;

R⁵ is hydrogen or lower alkyl;

R⁶ and R⁷ are independently a direct bond or alkylene of from 1 to about 10 carbons;

R⁸ is hydrogen or lower alkyl;

P is a hydrophilic polymer; and

T is a targeting ligand which targets cells or receptors selected from the group consisting of myocardial cells, endothelial cells, epithelial cells, tumor cells and the glycoprotein GPIIb/IIIa receptor.

2. A compound according to Claim 1 wherein:

X¹ and X² are independently a linking group selected from the group consisting of -C(=X³)-, -C(=X³)-N(R⁸)-, -N(R⁸)-C(=X³)- and -C(=X³)-N(R⁸)-C(=X³)-;

R¹ is acyl of from about 10 to about 22 carbons;

R² is hydrogen;

R^3 is alkylene of from 1 to about 10 carbons;
 R^4 is acyl of from about 10 to about 22 carbons;
 R^5 is hydrogen;
 R^6 and R^7 are independent a direct bond or lower alkylene; and
 R^8 is hydrogen.

5

3. A compound according to Claim 2 wherein:

X^1 is $-C(=O)-NH-C(=O)-$;

X^2 is $-C(=O)-$;

R^1 is acyl of from about 15 to about 20 carbons;

R^3 is alkylene of from 1 to about 3 carbons;

R^4 is acyl of from about 15 to about 20 carbons; and

R^6 is a direct bond;

R^7 is lower alkylene.

10

4. A compound according to Claim 3 wherein:

R^1 is acyl of from about 17 to about 19 carbons;

R^3 is methylene;

R^4 is acyl of from about 17 to about 19 carbons; and

R^7 is ethylene.

15

5. A compound according to Claim 4 wherein:

R^1 and R^2 are acyl of about 18 carbons

20

6. A compound according to Claim 1 wherein said hydrophilic polymer is selected from the group consisting of polyalkyleneoxides, polyvinyl alcohol, polyvinylpyrrolidones, polyacrylamides, polymethacrylamides, polyphosphazenes, poly(hydroxyalkylcarboxylic acids) and polyoxazolidines.

25

7. A compound according to Claim 6 wherein said hydrophilic polymer comprises a polyalkyleneoxide.

Sub
B1

8. A compound according to Claim 7 wherein said hydrophilic polymer is selected from the group consisting of polyethylene glycol and polypropylene glycol.

9. A compound according to Claim 8 wherein said hydrophilic polymer is polyethylene glycol.

10. A compound according to Claim 8 wherein said hydrophilic polymer is PEG3400.

11. A compound according to Claim 1 wherein said targeting ligand comprises a peptide of the formula:



wherein:

m and n are independently an integer of from 1 to about 100;

Xaa and Zaa are independently selected from the group consisting of natural amino acids and synthetic amino acids;

Yaa is selected from Arginine, Homoarginine, and Lysine-N-acetimidate; and

with the proviso that when Xaa and Zaa are sulfur containing amino acids, Xaa and Zaa may be linked together via a disulfide linkage.

12. A compound according to Claim 11, wherein:

Xaa is Glycine;

Yaa is Arginine;

Zaa is Serine;

n is 1, 2 or 3; and

m is 1.

13. A compound according to Claim 12, wherein:

n is 3.

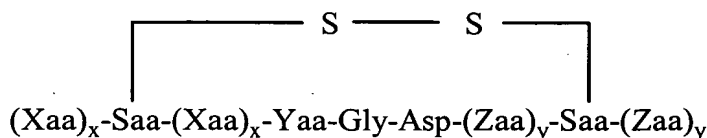
14. A compound according to Claim 11, wherein:

Sub
B1

Xaa and Zaa comprise an amino acid independently selected from sulfur containing amino acids.

15. A compound according to Claim 1 wherein said targeting ligand comprises a peptide of the following formula:

5



wherein:

each x and y is independently an integer of from 0 to about 50;

each Saa is selected from the group consisting of natural and synthetic sulfur containing amino acids;

10

each Xaa and Zaa are independently selected from the group consisting of natural amino acids and synthetic amino acids; and

Yaa is selected from Arginine, Homoarginine, and Lysine-N-acetimidate.

15

16. A compound according to Claim 15 wherein:

each Saa is independently selected from the group consisting of D-Cysteine, L- Cysteine, D-Penicillamine and L-Penicillamine.

20

17. A targeted vesicle composition for therapeutic or diagnostic use *in vivo* comprising, in an aqueous carrier, lipid, protein or polymer gas filled vesicles, wherein said vesicles further comprise a compound according to Claim 1.

18. A targeted vesicle composition according to Claim 17, wherein said vesicles are selected from the group consisting of liposomes and micelles.

19. A targeted vesicle composition according to Claim 18, wherein said vesicles comprise liposomes.

20. A targeted vesicle composition according to Claim 19 wherein said liposomes comprise a phospholipid selected from the group consisting of phosphatidylcholine, phosphatidylethanolamine and phosphatidic acid.

5 21. A targeted vesicle composition according to Claim 20 wherein said phosphatidylcholine is selected from the group consisting of dioleoylphosphatidylcholine, dimyristoylphosphatidylcholine, dipalmitoylphosphatidylcholine and distearoylphosphatidylcholine.

22. A targeted vesicle composition according to Claim 21 wherein said phosphatidylcholine comprises dipalmitoylphosphatidylcholine.

10 23. A targeted vesicle composition according to Claim 20 wherein said phosphatidylethanolamine is selected from the group consisting of dipalmitoylphosphatidylethanolamine, dioleoylphosphatidylethanolamine, N-succinyldioleoylphosphatidylethanolamine and 1-hexadecyl-2-palmitoylglycerophosphoethanolamine.

15 24. A targeted vesicle composition according to Claim 23 wherein said phosphatidylethanolamine comprises dipalmitoylphosphatidylethanolamine.

25. A targeted vesicle composition according to Claim 20 wherein said phosphatidic acid comprises dipalmitoylphosphatidic acid.

20 26. A targeted vesicle composition according to Claim 17, wherein said vesicles comprise a gas selected from the group consisting of perfluorocarbons and sulfur hexafluoride.

27. A targeted vesicle composition according to Claim 26 wherein said perfluorocarbon gas is selected from the group consisting of perfluoromethane, perfluoroethane, perfluoropropane, perfluorobutane and perfluorocyclobutane.

25 28. A targeted vesicle composition according to Claim 27 wherein said perfluorocarbon gas is selected from the group consisting of perfluoropropane and

Sub
B1

perfluorobutane.

29. A targeted vesicle composition according to Claim 28 wherein said perfluorocarbon gas comprises perfluorobutane.

~~30. A targeted vesicle composition according to Claim 17 wherein said gas is derived, at least in part, from a gaseous precursor.~~

31. A targeted vesicle composition according to Claim 30 wherein said gaseous precursor has a boiling point of greater than about 37°C.

32. A targeted vesicle composition according to Claim 31 wherein said gaseous precursor comprises a perfluorocarbon.

33. A targeted vesicle composition according to Claim 32 wherein said perfluorocarbon is selected from the group consisting of perfluoropentane and perfluorohexane.

34. A targeted vesicle composition according to Claim 17 wherein said vesicles further comprise a bioactive agent that is different from said gas and said compound.

35. A targeted vesicle composition according to Claim 34 wherein said bioactive agent comprises a therapeutic agent selected from the group consisting of genetic material, dihydroergotamine, heparin sulfate, tissue plasminogen activator, streptokinase, urokinase, hirudin, and mixtures thereof.

36. A method of imaging a thrombus in a region of a patient, said method comprising (i) administering to the patient a targeted vesicle composition according to Claim 17; and (ii) scanning said region of the patient with diagnostic imaging.

37. A method according to Claim 36, wherein said diagnostic imaging comprises diagnostic ultrasound.

38. A method according to Claim 37, wherein said region of a patient comprises the cardiac region.

39. A method of lysing a thrombus in a blood vessel comprising (i) administering to a patient, by intravenous injection, a targeted vesicle composition
5 according to Claim 17; (ii) scanning said patient with diagnostic imaging to visualize said thrombus; and (iii) applying ultrasonic energy to said thrombus.

40. A method of lysing a thrombus in a blood vessel comprising (i) administering to a patient, by intravenous injection, a targeted vesicle composition according to Claim 35; (ii) scanning said patient with diagnostic imaging to visualize said
10 thrombus; and (iii) applying ultrasonic energy to said thrombus.

41. A method for providing an image of an internal region of a patient comprising (i) administering to the patient a targeted vesicle composition according to Claim 17; and (ii) scanning the patient using ultrasound to obtain a visible image of the region.

42. A method according to Claim 41 wherein said targeting ligand
15 targets regions of arteriosclerosis.

43. A method according to Claim 41 wherein said arteriosclerosis comprises atherosclerotic plaque.

44. A method according to Claim 41 wherein said targeting ligand
20 targets infarcted myocardium.

45. A method according to Claim 41 wherein said targeting ligand targets cancer cells.

46. A method for diagnosing the presence of diseased tissue in a patient comprising (i) administering to the patient a targeted vesicle composition according to

Claim 17; and (ii) scanning the patient using ultrasound to obtain a visible image of the region.

47. A method according to Claim 46 wherein said targeting ligand targets regions of arteriosclerosis.

5 48. A method according to Claim 47 wherein said arteriosclerosis comprises atherosclerotic plaque.

49. A method according to Claim 46 wherein said targeting ligand targets infarcted myocardium.

10 50. A method according to Claim 46 wherein said targeting ligand targets cancer cells.

51. A method for the therapeutic delivery *in vivo* of a bioactive agent comprising (i) administering to a patient a therapeutically effective amount of a targeted vesicle composition according to Claim 34; and (ii) applying ultrasonic energy to the patient to release said bioactive agent from said targeted vesicles.

15 52. A method according to Claim 51, wherein said ultrasonic energy causes said vesicles to rupture.

53. A method according to Claim 51, further comprising the step of scanning the patient with diagnostic imaging to visualize the vesicles at the target site.

add
AL